

Drugs

DEPARTMENT OF HEALTH AND HUMAN SERVICES

Food and Drug Administration

[Docket No. 02D-0492]

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Certifier C. Penley

Draft Guidance for Industry and Reviewers on Estimating the Safe Starting Dose in Clinical Trials for Therapeutics in Adult Healthy Volunteers; Availability

AGENCY: Food and Drug Administration, HHS.

ACTION: Notice.

SUMMARY: The Food and Drug Administration (FDA) is announcing the availability of a draft guidance for industry and reviewers entitled “Estimating the Safe Starting Dose in Clinical Trials for Therapeutics in Adult Healthy Volunteers.” This draft guidance outlines a common process (algorithm) and terminology for deriving a maximum recommended starting dose for “first in human” clinical trials of new molecular entities in adult healthy volunteers. Described in the guidance is a method for using nonclinical data to select a maximum starting dose in adult humans that is not expected to result in significant toxicity. The goal is to ensure the safety of adult human volunteers in initial clinical trials.

DATES: Submit written or electronic comments on the draft guidance by *[insert date 60 days after date of publication in the **Federal Register**]*. General comments on agency guidance documents are welcome at any time.

ADDRESSES: Submit written requests for single copies of the draft guidance to the Division of Drug Information (HFD-240), Center for Drug Evaluation and Research, Food and Drug Administration, 5600 Fishers Lane, Rockville, MD

20857. Send two self-addressed adhesive labels to assist that office in processing your requests. Submit written comments on the draft guidance to the Dockets Management Branch (HFA-305), Food and Drug Administration, 5630 Fishers Lane, rm. 1061, Rockville, MD 20852. Submit electronic comments to <http://www.fda.gov/dockets/ecomments>. See the **SUPPLEMENTARY INFORMATION** section for electronic access to the draft guidance document.

FOR FURTHER INFORMATION CONTACT: Robert E. Osterberg, Center for Drug Evaluation and Research (HFD-24), Food and Drug Administration, 1451 Rockville Pike, Rockville, MD 20852, 301-594-5482 or M. David Green, Center for Biologics Evaluation and Research (HFM-579), Food and Drug Administration, 1401 Rockville Pike, Rockville, MD 20852, 301-827-5349.

SUPPLEMENTARY INFORMATION:

I. Background

FDA is announcing the availability of a draft guidance for industry and reviewers entitled “Estimating the Safe Starting Dose in Clinical Trials for Therapeutics in Adult Healthy Volunteers.” When selecting the starting dose in an initial clinical trial for a new molecular entity (NME), one can only rely on the safety data generated in nonclinical studies since, by definition, there are no human data. The draft guidance describes a method by which a starting dose may be selected for an initial clinical trial that is not expected to result in significant toxicity, but that will allow reasonably rapid attainment of phase I trial objectives (e.g., assessment of the NME’s tolerability, pharmacodynamic and/or pharmacokinetic profile). The draft guidance establishes a consistent terminology for discussing the starting dose and a strategy for selecting a maximum recommended safe starting dose based on no-observed-adverse-effect

levels in animals. Common conversion factors for deriving human equivalent doses from animal data are provided, and factors to be considered in determining reasonable safety margins are discussed in detail. The draft guidance also addresses the use of the nonclinical pharmacologically active dose and systemic exposure data in selection of a maximum recommended clinical starting dose. Comments on dose escalation are outside the scope of this draft document.

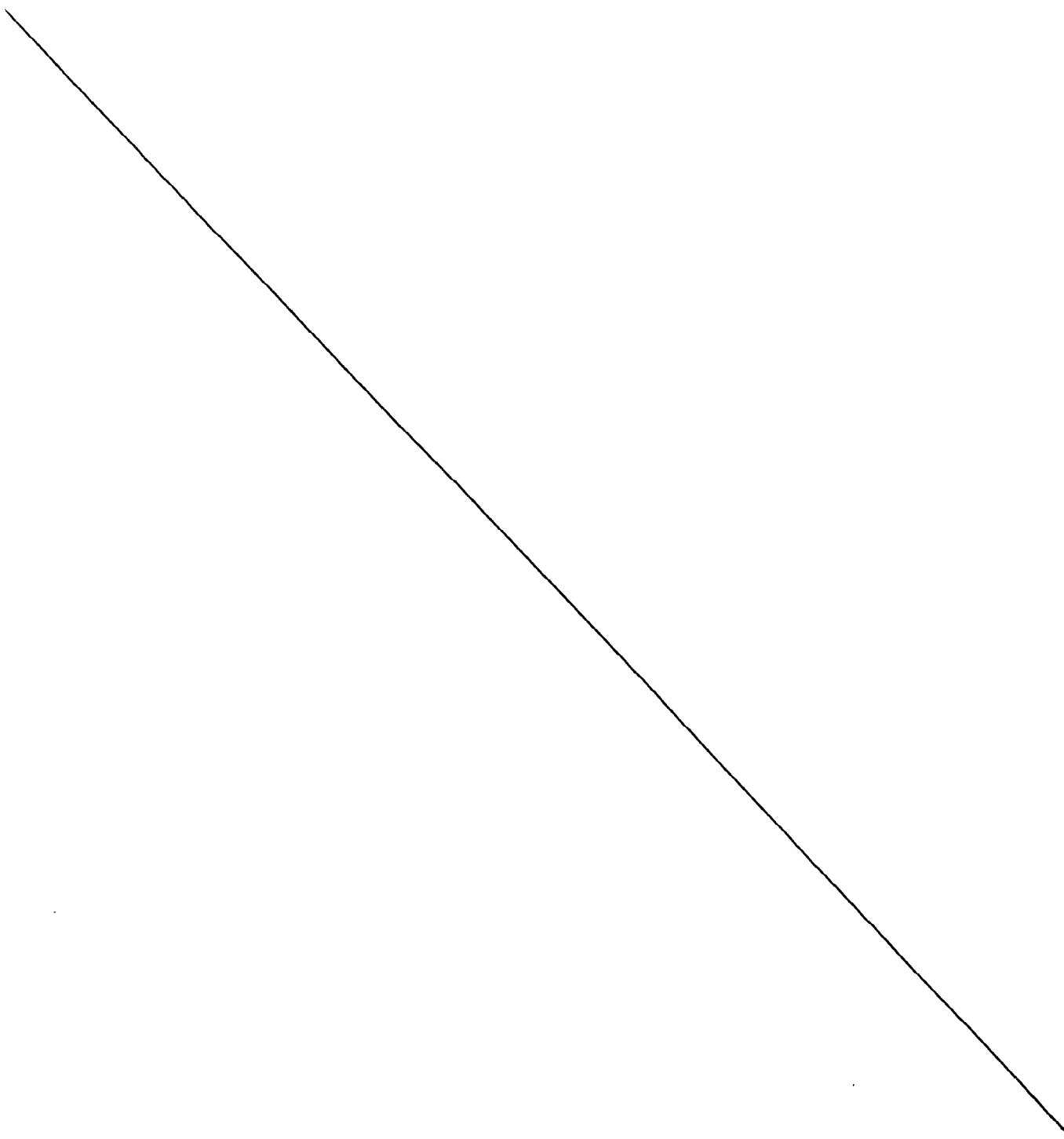
This draft guidance is being issued consistent with FDA's good guidance practices regulation (21 CFR 10.115). The draft guidance, when finalized, will represent the agency's current thinking on estimating a maximum safe starting dose in initial clinical trials for therapeutics in adult healthy volunteers. It does not create or confer any rights for or on any person and does not operate to bind FDA or the public. An alternative approach may be used if such approach satisfies the requirements of the applicable statutes and regulations.

II. Comments

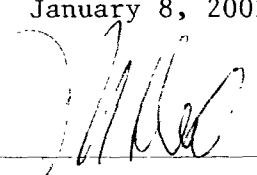
Interested persons may submit to the Dockets Management Branch (see **ADDRESSES**) written or electronic comments on the draft guidance. Two copies of mailed comments are to be submitted, except that individuals may submit one copy. Comments are to be identified with the docket number found in brackets in the heading of this document. The draft guidance and received comments are available for public examination in the Dockets Management Branch between 9 a.m. and 4 p.m., Monday through Friday.

III. Electronic Access

Persons with access to the Internet may obtain the document at either <http://www.fda.gov/cder/guidance/index.htm> or <http://www.fda.gov/ohrms/dockets/default.htm>.



Dated:

1/8/03
January 8, 2003.

Margaret M. Dotzel,
Assistant Commissioner for Policy.

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